PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

To:

Commissioner
US Department of Commerce
United States Patent and Trademark Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 28 June 2001 (28.06.01)	
International application No. PCT/US00/25609	**Applicant's or agent's file reference** AL01071K
International filing date (day/month/year) 19 September 2000 (19.09.00)	**Priority date** (day/month/year) 22 September 1999 (22.09.99)
Applicant HEITHOFF, Kim, Allen	

1. The designated Office is hereby notified of its election made:

[X] in the demand filed with the International Preliminary Examining Authority on:

15 March 2001 (15.03.01)

[ ] in a notice effecting later election filed with the International Bureau on:

2. The election [X] was

[ ] was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Charlotte ENGER

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

PCT

REC'D 17 JAN 2002

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
AL01071K		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/25609	19/09/2000	22/09/1999
International Patent Classification (IPC) or national classification and IPC A61K31/00		
Applicant SCHERING CORPORATION et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15/03/2001	15.01.2002
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Domingues, H Telephone No. +49 89 2399 7810

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25609

I. Basis of the r port

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-13	as originally filed

Claims, No.:

1-8	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-2, 4-7.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-2,4-7 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-2,4-7.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	3 and 8
Inventive step (IS)	Yes:	Claims	
	No:	Claims	3 and 8
Industrial applicability (IA)	Yes:	Claims	see separate sheet

No: Claims

2. Citations and explanations
see separate sheet

1. Concerning section III

Lack of clarity, Art. 6 PCT

As stated in the International Search Report (ISR), **claims 1-8** relate to therapeutic applications which are not clearly defined. Particularly, the definitions "for substantially returning work-related performance....." and "for substantially returning workplace productivity....." cannot be regarded as therapeutic indications and therefore the present set of claims lacks clarity under Art. 6 PCT. Since the ISR is limited to the use of desloratadine for the treatment of the diseases mentioned in claims 3 and 8, the observations under section V (see below) concern only the use of said compound for the treatment of said diseases.

2. Concerning section V

2.1 The following documents cited in the International Search Report were taken into account:

*D1: HANDLEY DEAN A ET AL: 'Methods for treating dermatitis using descarboethoxyloratadine.' 25 April 2000 (2000-04-25) , OFFICIAL GAZETTE OF THE UNITED STATES PATENT AND TRADEMARK OFFICE, VOL. 1233, NR. 4, PAGE(S) NO PAGINATION , APR. 25, 2000 XP000997862 ISSN: 0098-1133
D2: WO 98 48803 A (SHIBAHARA TAKESHI ;KASE KOICHIRO (JP); KAMI HIROSHI (JP); OKAZAKI) 5 November 1998 (1998-11-05) & EP 0 978 281 A 9 February 2000 (2000-02-09)
D3: US-A-5 900 421 (HANDLEY DEAN A ET AL) 4 May 1999 (1999-05-04)
D4: WO 98 34614 A (SEPRACOR INC) 13 August 1998 (1998-08-13)
D5: US-A-4 659 716 (VILLANI FRANK J ET AL) 21 April 1987 (1987-04-21)
D6: WO 98 06394 A (SCHERING CORP) 19 February 1998 (1998-02-19)
D7: US-A-5 595 997 (ABERG A K GUNNAR ET AL) 21 January 1997 (1997-01-21)
D8: MOLET, S. ET AL: 'Inhibitory activity of loratadine and descarboxyethoxyloratadine on histamine-induced activation of endothelial cells' CLIN. EXP. ALLERGY (1997), 27(10), 1167-1174 , XP000997866
D9: GENOVESE: 'loratadine and desethoxycarbonyl loratadine...' CLINICAL AND EXPERIMENTAL ALLERGY, vol. 27, no. 5, 1997, pages 559-567, XP000998792

*This document would become relevant if the present application were found not to enjoy a

valid priority date.

2.2 Industrial applicability, Art. 33(4)PCT

For the assessment of the present **claims 1-8** on the question of whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

2.3 Novelty (Art 33(2)PCT) and inventive step (Art. 33(3)PCT)

The use of desloratadine for the treatment of different types of allergic and inflammatory diseases is well documented in the prior art. **D3** discloses desloratadine as an antihistaminic that avoids the adverse side-effects associated with other antihistamines. Desloratadine is said to be efficient in the treatment of seasonal allergic and perennial rhinitis, chronic urticaria, allergic asthma and dermatitis (see abstract, columns 1-3 and claims). The use of desloratadine for the treatment of histamine-induced disorders, dermographism or dermatitis and allergic rhinitis (see pg. 1-2 and claims) is described in **D4** and **D7**. **D5** (see abstract and claims), **D8** and **D9** (see introduction and results in both documents) also disclose the antihistaminic activity and antiallergic properties of desloratadine.

From the discussion above, it is clear that the use of desloratadine for the treatment of the diseases mentioned in claims 3 and 8 is known from the prior art. Therefore, novelty (Art. 33(2) PCT) and inventive step (Art. 33(3)PCT) cannot be acknowledged for these claims.

PATENT COOPERATION TREATY

Attempted To
Date: 2/1/02 Initials: cer

PATENT DEPARTMENT
RECEIVED
JAN 2 3 2002
ROUTE TO
COMMENTS
☑ COMPUTER INPUT
☐ RZA
☐ DEBIT NOTE ENTERED
COMPLETED BY 1/25/02

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

HOFFMAN, Thomas D.
Schering-Plough Corporation
Patent Department K-6-1 1990
2000 Galloping Hill Road
Kenilworth, NJ 07033-0530
ETATS-UNIS D'AMERIQUE

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	15.01.2002
Applicant's or agent's file reference AL01071K	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/25609	19/09/2000	22/09/1999

Applicant
SCHERING CORPORATION et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/	Authorized officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Exner, K Tel.+49 89 2399-7826

Form PCT/IPEA/416 (July 1992)

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
AL01071K		
International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US00/25609	19/09/2000	22/09/1999
International Patent Classification (IPC) or national classification and IPC A61K31/00		
Applicant SCHERING CORPORATION et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the report
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations suporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
15/03/2001	15.01.2002
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Domingues, H Telephone No. +49 89 2399 7810

Form PCT/IPEA/409 (cover sheet) (January 1994)

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US00/25609

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:
Description, pages:

1-13	as originally filed

Claims, No.:

1-8	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 1-2, 4-7.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-2,4-7 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 1-2,4-7.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	3 and 8
Inventive step (IS)	Yes:	Claims	
	No:	Claims	3 and 8
Industrial applicability (IA)	Yes:	Claims	see separate sheet

No: Claims

2. Citations and explanations
see separate sheet

1. Concerning section III

Lack of clarity, Art. 6 PCT

As stated in the International Search Report (ISR), **claims 1-8** relate to therapeutic applications which are not clearly defined. Particularly, the definitions "for substantially returning work-related performance....." and "for substantially returning workplace productivity....." cannot be regarded as therapeutic indications and therefore the present set of claims lacks clarity under Art. 6 PCT. Since the ISR is limited to the use of desloratadine for the treatment of the diseases mentioned in claims 3 and 8, the observations under section V (see below) concern only the use of said compound for the treatment of said diseases.

2. Concerning section V

2.1 The following documents cited in the International Search Report were taken into account:

*D1: HANDLEY DEAN A ET AL: 'Methods for treating dermatitis using descarboethoxyloratadine.' 25 April 2000 (2000-04-25) , OFFICIAL GAZETTE OF THE UNITED STATES PATENT AND TRADEMARK OFFICE, VOL. 1233, NR. 4, PAGE(S) NO PAGINATION , APR. 25, 2000 XP000997862 ISSN: 0098-1133
D2: WO 98 48803 A (SHIBAHARA TAKESHI ;KASE KOICHIRO (JP); KAMI HIROSHI (JP); OKAZAKI) 5 November 1998 (1998-11-05) & EP 0 978 281 A 9 February 2000 (2000-02-09)
D3: US-A-5 900 421 (HANDLEY DEAN A ET AL) 4 May 1999 (1999-05-04)
D4: WO 98 34614 A (SEPRACOR INC) 13 August 1998 (1998-08-13)
D5: US-A-4 659 716 (VILLANI FRANK J ET AL) 21 April 1987 (1987-04-21)
D6: WO 98 06394 A (SCHERING CORP) 19 February 1998 (1998-02-19)
D7: US-A-5 595 997 (ABERG A K GUNNAR ET AL) 21 January 1997 (1997-01-21)
D8: MOLET, S. ET AL: 'Inhibitory activity of loratadine and descarboxyethoxyloratadine on histamine-induced activation of endothelial cells' CLIN. EXP. ALLERGY (1997), 27(10), 1167-1174 , XP000997866
D9: GENOVESE: 'loratadine and desethoxycarbonyl loratadine...' CLINICAL AND EXPERIMENTAL ALLERGY, vol. 27, no. 5, 1997, pages 559-567, XP000998792

*This document would become relevant if the present application were found not to enjoy a

valid priority date.

2.2 Industrial applicability, Art. 33(4)PCT

For the assessment of the present **claims 1-8** on the question of whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

2.3 Novelty (Art 33(2)PCT) and inventive step (Art. 33(3)PCT)

The use of desloratadine for the treatment of different types of allergic and inflammatory diseases is well documented in the prior art. **D3** discloses desloratadine as an antihistaminic that avoids the adverse side-effects associated with other antihistamines. Desloratadine is said to be efficient in the treatment of seasonal allergic and perennial rhinitis, chronic urticaria, allergic asthma and dermatitis (see abstract, columns 1-3 and claims). The use of desloratadine for the treatment of histamine-induced disorders, dermographism or dermatitis and allergic rhinitis (see pg. 1-2 and claims) is described in **D4** and **D7**. **D5** (see abstract and claims), **D8** and **D9** (see introduction and results in both documents) also disclose the antihistaminic activity and antiallergic properties of desloratadine.

From the discussion above, it is clear that the use of desloratadine for the treatment of the diseases mentioned in claims 3 and 8 is known from the prior art. Therefore, novelty (Art. 33(2) PCT) and inventive step (Art. 33(3)PCT) cannot be acknowledged for these claims.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 March 2001 (29.03.2001)

PCT

(10) International Publication Number
WO 01/21162 A2

(51) International Patent Classification[7]: A61K 31/00

(21) International Application Number: PCT/US00/25609

(22) International Filing Date:
19 September 2000 (19.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/400,599 22 September 1999 (22.09.1999) US

(71) Applicant *(for all designated States except US)*: SCHERING CORPORATION [US/US]; 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 (US).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)*: HEITHOFF, Kim, Allen [US/US]; 22 Williams Street, P.O. Box 423, Oldwick, NJ 08858-0423 (US).

(74) Agent: HOFFMAN, Thomas, D.; Schering-Plough Corporation, Patent Department, K-6-1 1990, 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *Without international search report and to be republished upon receipt of that report.*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/21162 A2

(54) Title: TREATING ALLERGIC AND INFLAMMATORY CONDITIONS

(57) Abstract: The use of desloratadine for the preparation of a medicament for substantially returning work-related performance and/or workplace productivity of a person suffering from an allergic and/or inflammatory condition of the skin airway passages, e.g., season allergic rhinitis, perennial allergic rhinitis, atopic dermatitis, urticaria or allergic asthma to the person's baseline w rk-related performance and baseline workplace productivity.

TREATING ALLERGIC AND INFLAMMATORY CONDITIONS

BACKGROUND OF THE INVENTION

This invention relates to the use of desloratadine for the preparation of a medicament for substantially returning work-related performance and/or workplace productivity of a patient suffering from an allergic and/or inflammatory condition to the person's baseline work-related performance and baseline workplace productivity.

The symptoms and side effects of an allergic and/or inflammatory condition of the skin or upper and lower airway passages such as seasonal allergic rhinitis ("SAR") include itchy, watery eyes, sneezing, runny nose, nasal congestion, urticaria, sommolence and general malaise. The pharmacologic effects of treating allergic and/or inflammatory condition such as SAR with sedating antihistamines include sommolence, blurred vision, dry mouth and individual performance impairment at home, in school and at work as well as impairment of workplace productivity. SAR affects up to 45 million people in the United States and many more millions worldwide.

Cockurn, Iain M, et al., in Business & Health, March 1999, pages 49-50 and in J Occup Eniviron Med., November 1999, Vol. 41(11), pages 948-953 disclose treating allergic reactions with sedating antihistamines, alone or in combination with decongestants, leads to impaired individual performance and decreased workplace productivity of workers compared to treatment with non-sedating antihistamines.

In view of the high prevalence of SAR, even relatively small effects on individual performance will have a significant impact on work-related performance and workplace productivity in the worldwide population, Thus, there is a need for a clinically more effective therapy for treating/preventing an allergic and or inflammatory condition of the skin and upper or lower airway passages in workers while simultaneously enhancing their work-related performance as well as their workplace productivity.

SUMMARY OF THE INVENTION

The present invention provides a method of substantially returning the work-related performance of a person suffering from an allergic and/or inflammatory condition of the skin or airway passages to the person's baseline work-related performance which comprises administering an amount of desloratadine to said person effective for such returning.

The present invention provides a method of returning workplace productivity of a person suffering from an allergic and/or inflammatory condition of the skin or airway passages to the person's baseline workplace productivity which comprises administering an effective amount of desloratadine to said person effective for such returning.

In a preferred embodiment, the present invention provides a method of substantially returning work-related performance of a person suffering from seasonal allergic rhinitis to the person's baseline work-related performance which comprises administering an amount of desloratadine to such person effective for such returning.

In a preferred embodiment, the present invention provides a method of substantially returning workplace productivity of a person suffering from seasonal allergic rhinitis to the person's baseline workplace productivity which comprises administering an amount of desloratadine to said person effective for such returning.

In another preferred embodiment, the present invention provides a method of enhancing work-related performance of a patient suffering from atopic dermatitis or urticaria which comprises administering an amount of desloratadine effective for such enhancing.

In another preferred embodiment, the present invention provides a method of substantially returning workplace productivity of a person suffering from atopic dermatitis or urticaria to the person's baseline work-related performance to the person's baseline work-related performance which comprises administering an amount of desloratadine effective for such returning.

In another preferred embodiment, the present invention provides a method of returning performance of a person suffering from atopic dermatitis or urticaria to

the person's baseline workplace productivity which comprises administering an amount of desloratadine to said person effective for such returning.

In another preferred embodiment, the present invention provides a method of substantially returning workplace productivity of a person suffering from an allergic and/ or inflammatory condition of the skin or passages to the person's baseline workplace productivity by administering an initial amount of desloratadine to said person effective for such returning.

In another preferred embodiment, the present invention provides a method ~~of substantially returning performance of a person suffering from an allergic and/~~ or inflammatory condition of the skin or airway passages to the person's baseline workplace productivity by administering an initial amount of desloratadine to said person effective for such returning.

The invention also contemplates pharmaceutical compositions for substantially returning work-related performance and/or workplace productivity of a person suffering from an allergic and/or inflammatory condition of the skin or airway passage to the person's baseline work-related performance and/or workplace performance comprising an amount of desloratadine effective for such returning.

DETAILED DESCRIPTION OF THE INVENTION

Persons afflicted with the symptoms and side effects of an allergic and/or inflammatory condition of the skin and upper or lower airway passages -such as seasonal allergic rhinitis- who are treated with an initial effective amount of desloratadine exhibit a significantly higher work-related performance and a significantly higher workplace productivity in a controlled clinical setting compared to untreated persons as well as with persons treated with an initial standard dose of the sedating antihistamine, diphenhydramine.

The phrase "the person's baseline work-related performance" as used herein means the person's work-related performance at a time prior to the person's exhibiting signs and/or symptoms of allergic and/or inflammatory conditions of the skin or airway passages as measured by art-recognized methods hereinafter d scribed.

The phrase "the person's baseline workplace productivity" as used herein means the person's baseline workplace productivity as used herein means the person's performance at a time prior to the person's exhibiting the signs and/or symptoms of allergic and/or inflammatory conditions of the skin or airway passages as measured by art-recognized methods hereinafter described.

The phrase "substantially returning" as used herein in reference to a person's baseline work-related performance or baseline workplace productivity means returning to within about 5-10%, preferably within about 5% and more preferably within about 1-2% of the baseline values.

The phrase "allergic and/ or inflammatory conditions of the skin or airway passages" as used herein means those allergic and/or inflammatory conditions and symptoms found on the skin and in the airway passages from the nose to the lungs. Typical allergic and/or inflammatory conditions of the skin and upper and lower airway passages include seasonal and perennial allergic rhinitis, non-allergic rhinitis, asthma including allergic and non-allergic asthma, sinusitis, colds (in combination with a NSAID, e.g., aspirin ibuprofen or APAP) and/or a decongestant e.g. pseudoephedrine), dermatitis, especially allergic and atopic dermatitis, and urticaria and symptomatic dermographism as well as retinophathy, and small vessel diseases, associated with diabetes mellitus.

The amount of desloratadine effective for treating or preventing allergic and/or inflammatory conditions of the skin and upper and lower airway passages will vary with the age, sex, body weight and severity of the allergic and inflammatory condition of the patient. Typically, the amount of desloratadine effective for treating or preventing such allergic and inflammatory conditions is in the range of about 2.5 mg/day to about 45 mg/day, preferably about 2.5 mg/day to about 20 mg/day, or about 4.0 mg/day to about 15 mg/day, or about 5.0 mg/day to about 10 mg/day, more preferably about 5.0 mg/day to about 7.5 mg/day, and most preferably about 5.0 mg/day in single or divided doses, e.g. two 2.5 mg doses, or about 5.0 mg/day in a single dose.

Desloratadine is a non-sedating long acting histamine antagonist with potent selectiv peripheral H1-receptor antagonist activity. Following oral administration, loratadine is rapidly metabolized to descarboethoxyloratadine or

desloratadine, a pharmacologically active metabolite. *In vitro* and *in vivo* animal pharmacology studies have been conducted to assess various pharmacodynamic effects of desloratadine and loratadine. In assessing antihistamine activity in mice (comparison of ED_{50} value), desloratadine was relatively free of producing alterations in behavior alterations in behavior, neurologic or autonomic function. The potential for desloratadine or loratadine to occupy brain H1-receptors was assessed in guinea pigs following i.p. administration and results suggest poor access to central histamine receptors for desloratadine or loratadine.

In vivo studies also suggest that an inhibitory effect of desloratadine on allergic bronchospasm and cough can also be expected.

The clinical efficacy and safety of desloratadine has been documented in over 3,200 seasonal allergic rhinitis patients in 4 double-blind, randomized clinical trials. The results of these chemical studies demonstrated the efficacy of desloratadine in the treatment of adult and adolescent patients with seasonal rhinitis.

Desloratadine is particularly useful for the treatment and prevention of the nasal (stuffiness/congestion, rhinorrhea, nasal itching, sneezing) and non-nasal (itchy/burning eyes, tearing/watery eyes, redness of the eyes, itching of the ears/palate) symptoms of seasonal allergic rhinitis, including nasal congestion, in patients in need of such treating and/ or preventing. Desloratadine may be used alone, or in combination with a decongestant, e.g., pseudeoephridine and/or an analgesic, e.g., a NSAID such as acetominophen or ibuprofen.

STUDY DESIGNS AND CONCEPTS

A series of randomized, double-blinded(treatment), placebo-controlled studies have been designed to quantify the impact of seasonal allergic rhinitis ("SAR") and SAR treatments on work-related performance and workplace productivity of subjects as measured by art-recognized selected areas of performance and workplace productivity. In one series of studies, the effects of SAR (burden of disease) in subjects will be quantified by comparing the work-related performance levels in asymptomatic SAR subjects to the work-r lated subjects performance levels in symptomatic SAR subjects. In another series of

studies, the differential impact following two different treatments for SAR on work-related performance of subjects will be quantified: the effects of desloratadine 5 mg tablets will be compared to diphenhydramine 50 mg (and placebo of each drug) among subjects with symptomatic SAR during exposure of the subjects to ragweed pollen. A consistent level of ragweed pollen exposure will be assured by conducting these studies in an environmental exposure unit (EEU). The baseline work-related performance and baseline workplace productivity of each subject will be measured at day 0 prior to exposure to ragweed pollen in the EEU.

WORK-RELATED PERFORMANCE TESTS

The work-related performance abilities of the subjects to be examined in one study series were selected based on the consensus of an expert panel consisting of neuropsychologists, industrial psychologists, and allergists. These work-related performance abilities cover the domains thought to be most affected by the symptoms of SAR and/or by sedation caused by SAR treatments. In addition, the expert panel prioritized those performance domains that are most closely related to abilities associated with safety and productivity. The work-related performance abilities were then mapped by the expert panel to neuropyschological performance tests.

PRIMARY ENDPOINT:

The effects of SAR(also called the burden of disease) will be measured by measuring the selective attention in asymptomatic versus symtomatic subjects and in symptomatic subjects treated with desloratadine 5 mg tablets versus symptomatic subjects treated diphenhydramine 50 mg.

Performance Domain	Definition	Performance Measure
Selective Attention	The ability to concentrate and not be distracted while performing a task over a period of time.	Kay Continuous Performance Test (Omission Errors Score)

SECONDARY ENDPOINTS:

1. Impact of Treatment (Desloratadine vs. Diphenhydramine) will be determined by measuring the perceptual speed in asymptomatic versus symtomatic subjects and in symptomatic subjects treated with desloratadine 5 mg tablets versus symptomatic subjects treated diphenhydramine 50 mg.

Performance Domain	Definition	Performance Measure
Perceptual Speed	The ability to quickly and accurately compare letters, numbers, objects, pictures or patterns. The things to be compared may be presented at the same time or one after the other. This ability also includes comparing a presented object with a remembered object	Automated Neuropsychological Matrices (ANAM) Running Memory CPT (Accuracy Score)
Near Vision	The ability to see details of objects at a close range (within a few feet of the observer).	CogScreen Visual Sequence Comparison (Accuracy Score)

2. Burden of Disease will be measured in asymptomatic vs. symptomatic subjects; and in symptomatic subjects vs. those treated with Desloratadine by measuring the information ordering as follows:

Performance Domain	Definition	Performance Measure
Information Ordering	The ability to follow a given set of rules or instructions in order to arrange things or actions in a certain order. The things or actions can include numbers, letters, words, pictures, procedures, sentences, and mathematical or logical operations.	CogScreen Digit Symbol Coding (with Delay) (Response Time Score)

3. **OTHER ENDPOINTS:**

Additional measures of some of the performance domains will also be included as secondary endpoints. These include, but are not limited to, problem sensitivity, memorization, number facility, time sharing, and response orientation, and rate control.

INCLUSION AND EXCLUSION CRITERIA

Finally, standard inclusion and exclusion criteria will be used to assure that other factors, such as nicotine and/or alcohol use or sleep disturbances, are not contributing to any observed effect.

ENVIRONMENTAL EXPOSURE UNIT (EEU)

The EEU is a scientifically recognized pollen exposure system that has been used to evaluate the efficacy of anti-allergic medications, including determinations of the "onset of action" of these medications to relieve the signs and symptoms of pollen-induced allergic rhinitis. The controlled exposure to an aeroallergen, usually short ragweed pollen, has eliminated variables associated with other methods of clinical evaluation of these medications. The clinical relevance of the results of this test system have been validated by comparison of

the results of clinical trails in this unit with those of other modes of allergen challenge, in particular exposure of allergic subjects to natural environmental increases in pollen levels.

Prior to those study days when the subjects are to be symptomatic and will undergo work-related performance and work-place productivity testing, they will be exposed during two to six priming sessions of 3 hours each to controlled pollen levels (3500 ± 500 grains/m^3) in the EEU. Subjects will record symptom severity every 30 minutes until the symptom severity criteria for enrollment in the study are met or the 3 hours have lapsed following which they will be transferred to a pollen-free room for up to one hour of observation. Subjects whose symptoms are so severe that they cannot remain in the EEU for at least 3 hours are moved to a pollen-free room and discharged from the study. To qualify for enrollment the subjects are required to achieve a total SAR symptom severity score of ≥10 made up of a nasal symptom score of ≥6 and of ≥4 for the non-nasal symptoms. On leaving the EEU those subjects who meet the severity scores inclusion criteria will be assigned to computer-generated randomization.

On the Baseline (symptomatic) and treatment-study days the enrolled subjects will report to the EEU at 7:30 AM. They will complete the daily baseline pre-exposure evaluation of their SAR symptom severity at 8:00 AM, following which they will begin exposure to ragweed pollen (3500±500 grain/m^3) for 8 hours, i.e., from 8:00 AM to 4:00 PM. Promptly following symptom severity ratings at 9:30 AM, the subjects will be evaluated for qualification for dosing and continuation in the study. Immediately after completing the 10:00 AM dairy card, all subjects will take their medications with a glass (180 mL) of water.

The work-related performance and work-place productivity testing will begin approximately 1 ½ hours after the initial dosing and will continue until approximately 2 hours after the initial dosing. This timing will allow for testing to be completed during the time that the two drugs are expected to show efficacy.

WORK-PLACE PRODUCTIVITY TESTS

The work-place productivity tests selected will be based on their sensitivity to the effects of sedation and seasonal allergic rhinitis symptoms, and

their relevance to the skills required for word processing. The same subject inclusion/exclusion criteria used for the work-related performance studies will be used. A consistent level of ragweed pollen exposure will be assured by conducting these studies in the above-described environmental exposure unit (EEU).

PRIMARY STUDY OBJECTIVE:

To show that work-place productivity is higher when subjects with symptomatic SAR are treated with desloratadine, 5 mg tablets antihistamine, than when subjects are treated with diphenhydramine 50 mg, a sedating antihistamine after exposure of both sets of subjects to ragweed pollen in an above-described EEU.

SECONDARY STUDY OBJECTIVES:

1. To show that work-related performance and workplace productivity are higher when subjects with symptomatic SAR are treated with desloratadine than when they are not treated; and
2. To show that SAR negatively impacts workplace productivity.

RESEARCH BACKGROUND FOR THE STUDIES

The hypotheses that relate to the objectives for these studies are based on the documented findings that dosing with diphenhydramine causes somnolence and impairment of cognitive and psychomotor functions and vigilance and intuitive projections, and that the signs and symptoms of SAR adversely affect those same functions. SAR may exert its impairing effects not only by affecting visual and auditory responses and upper airway breathing capacity but also by a sense of general malaise and discomfort. These impairments of work-related performance should result in diminished workplace productivity.

The study subjects, who will have a history of ragweed pollen associated SAR and a documented positive skin test to short ragweed pollen, will be evaluated while asymptomatic and symptomatic to establish baseline work-related

performance and workplace productivity data to meet the study objectives. Because these subjects will be evaluated for the effects of their SAR signs and symptoms and of the two study medications on individual performance and workplace productivity, they will need to meet at least minimal requirements for typing/word processing skills.

Both medications (desloratadine and diphenhydramine) are expected to relieve the signs and symptoms of SAR during the course of the treatment study day, beginning as soon as one-and-one half-hours after dosing and continuing during the testing periods.

GENERAL EXPERIMENTAL

U.S.Patent No. 4,659,716 discloses desloratadine as a non-sedating antihistamine as well as methods of making desloratadine, pharmaceutical compositions containing it and methods of using desloratadine and pharmaceutical compositions containing it to treat allergic reaction in mammals.

U.S.Patent No. 5,595,997 discloses pharmaceutical compositions containing desloratadine and methods of using desloratadine for treating allergic rhinitis.

Desloratadine is available from Schering Corporation, Kenilworth, N.J. Diphenhydramine is available under the BENADRYL trademark on a non-prescription basis.

The pharmaceutical compositions of desloratadine be adapted for any mode of administration e.g., for oral, parenteral, e.g., subcutaneous ('SC"), intramuscular ("IM"), intravenous ("IV") and intraperitoneal ("IP"), topical or vaginal administration or by inhalation (orally or intranasally). Preferably desloratadine is administered orally.

Such compositions may be formulated by combining desloratadine or an equivalent amount of a pharmaceutically acceptable salt thereof with a suitable, inert, pharmaceutically acceptable carrier or diluent which may be either solid or liquid. Desloratadine may be converted into the pharmaceutically acceptable acid addition salts by admixing it with an equivalent amount of a pharmaceutically acceptable acid. Typically suitable pharmaceutically acceptable acids include the mineral acids, .g., HNO_3, H_2SO_4, H_3PO_4, HCl, HBr, organic acids, including, but

not limited to, acetic, trifluoroacetic, propionic, lactic, maleic, succinic, tartaric, glucuronic and citric acids as well as alkyl or arylsulfonic acids, such as p-toluenesulfonic acid, 2-naphthalenesulfonic acid, or methanesulfonic acid. The preferred pharmaceutically acceptable salts are trifluoroacetate, tosylate, mesylate, and chloride. Desloratadine is more stable as the free base than as an acid addition salt and the use of the desloratadine free base in pharmaceutical compositions of the present invention is more preferred.

Solid form compositions include powders, tablets, dispersible granules, capsules, cachets and suppositories. The powders and tablets may be comprised of from about 5 to about 95 percent active ingredient. Suitable solid carriers are known in the art, e.g. magnesium carbonate, magnesium stearate, talc, sugar or lactose. Tablets, powders, cachets and capsules can be used as solid dosage forms suitable for oral administration. Examples of pharmaceutically acceptable carriers and methods of manufacture for various compositions may be found in A. Gennaro (ed.), Remington's Pharmaceutical Sciences, 18th Edition, (1990), Mack Publishing Co., Easton, Pennsylvania.

Liquid form preparations include solutions, suspensions and emulsions. As an example may be mentioned water or water-propylene glycol solutions for parenteral injection. Solid form preparations may be converted into liquid preparations shortly before use for either oral or administration. Parenteral forms to be injected intravenously, intramuscularly or subcutaneously are usually in the form of sterile solutions and may contain tonicity agents (salts or glucose), and buffers. Opacifiers may be included in oral solutions, suspensions and emulsions. Liquid form preparations may also include solutions for intranasal administration.

Aerosol preparations suitable for inhalation may include solutions and solids in powder form, which may be in combination with a pharmaceutically acceptable carrier, such as an inert compressed gas, e.g., nitrogen.

Also included are solid form preparations that are intended to be converted, shortly before use, to liquid form preparations for either oral or parenteral administration. Such liquid forms include solutions, suspensions and emulsions.

Desloratadine may also be deliverable transdermally. The transdermal compositions can take the form of creams, lotions, aerosols and/or emulsions and can be included in a transdermal patch of the matrix or reservoir type as are conventional in the art for this purpose.

Preferably, the pharmaceutical composition is in a unit dosage form. In such form, the preparation is subdivided into suitably sized unit doses containing appropriate quantities of desloratadine and other, if any active component, e.g., effective amounts to achieve the desired purpose.

WHAT is claimed:

(1) The use of desloratadine for the preparation of a medicament for substantially returning work-related performance of a person suffering from an allergic and/or inflammatory condition of the skin or airway passages to the person's baseline work-related performance.

(2) The use of desloratadine for the preparation of a medicament for substantially returning workplace productivity of a person suffering from an allergic and/or inflammatory condition of the skin or airway passages to the person's baseline workplace productivity.

(3) The use of desloratadine for the preparation of a medicament for substantially returning work-related performance of a person suffering from seasonal or perennial allergic rhinitis to the person's baseline work-related performance.

(4) The use of any preceding claim wherein the amount of desloratadine is about 2.5 mg/day to about 45 mg/day.

(5) The use of any preceding claim wherein the amount of desloratadine is about 5 mg/day to about 15 mg/day.

(6) The use of any preceding claim wherein the amount of desloratadine is about 5 mg/day to about 10 mg/day.

(7) The use of any preceding claim wherein the amount of desloratadine is about 5 mg/day.

(8) The use of any preceding claim wherein the allergic and/or inflammatory condition of the skin or airway passages is seasonal allergic rhinitis, perennial all rgic rhinitis, atopic dermatitis, urticaria or allergic asthma.

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
29 March 2001 (29.03.2001)

PCT

(10) International Publication Number
WO 01/21162 A3

(51) International Patent Classification[7]: A61K 31/4545, A61P 37/08, 29/00

(21) International Application Number: PCT/US00/25609

(22) International Filing Date:
19 September 2000 (19.09.2000)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
09/400,599 22 September 1999 (22.09.1999) US

(71) Applicant *(for all designated States except US)*: **SCHERING CORPORATION** [US/US]; 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 (US).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **HEITHOFF, Kim, Allen** [US/US]; 22 Williams Street, P.O. Box 423, Oldwick, NJ 08858-0423 (US).

(74) Agent: **HOFFMAN, Thomas, D.**; Schering-Plough Corporation, Patent Department, K-6-1 1990, 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 (US).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, MZ, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, US, UZ, VN, YU, ZA.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

(88) Date of publication of the international search report:
7 March 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/21162 A3

(54) Title: TREATING ALLERGIC AND INFLAMMATORY CONDITIONS USING DESLORATADINE

(57) Abstract: The use of desloratadine for the preparation of a medicament for substantially returning work-related performance and/or workplace productivity of a person suffering from an allergic and/or inflammatory condition of the skin airway passages, e.g., season allergic rhinitis, perennial allergic rhinitis, atopic dermatitis, urticaria or allergic asthma to the person's baseline work-related performance and baseline workplace productivity.

INTERNATIONAL SEARCH REPORT

Interna[redacted]pplication No
PCT/[redacted]00/25609

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/4545 A61P37/08 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, PAJ, WPI Data, CHEM ABS Data, EMBASE, SCISEARCH, BIOSIS, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	HANDLEY DEAN A ET AL: "Methods for treating dermatitis using descarboethoxyloratadine." 25 April 2000 (2000-04-25) , OFFICIAL GAZETTE OF THE UNITED STATES PATENT AND TRADEMARK OFFICE, VOL. 1233, NR. 4, PAGE(S) NO PAGINATION , APR. 25, 2000 XP000997862 ISSN: 0098-1133 the whole document ---	1,2,4-8
X	WO 98 48803 A (SHIBAHARA TAKESHI ;KASE KOICHIRO (JP); KAMI HIROSHI (JP); OKAZAKI) 5 November 1998 (1998-11-05) & EP 0 978 281 A 9 February 2000 (2000-02-09) table 2 page 2, line 10 - line 40 --- -/--	1-8

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
31 August 2001	06/09/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bonzano, C

Form PCT/ISA/210 (second sheet) (July 1992)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 900 421 A (HANDLEY DEAN A ET AL) 4 May 1999 (1999-05-04) column 3, paragraph 2 - paragraph 6	1,2,4-8
X	WO 98 34614 A (SEPRACOR INC) 13 August 1998 (1998-08-13) claims 1,14-24 page 2, line 28 -page 3, line 7	1-8
X	US 4 659 716 A (VILLANI FRANK J ET AL) 21 April 1987 (1987-04-21) column 1, line 17 - line 46 example 5	1-8
X	WO 98 06394 A (SCHERING CORP) 19 February 1998 (1998-02-19) page 3, line 30 -page 4, line 24 claims 7,8,13,14	1-8
X	US 5 595 997 A (ABERG A K GUNNAR ET AL) 21 January 1997 (1997-01-21) column 3, line 21 - line 47	1-8
X	MOLET, S. ET AL: "Inhibitory activity of loratadine and descarboxyethoxyloratadine on histamine-induced activation of endothelial cells" CLIN. EXP. ALLERGY (1997), 27(10), 1167-1174 , XP000997866 page 1168, column 1, paragraph 1 - paragraph 2 page 1173, column 1, paragraph 1	1,2,4-7
X	GENOVESE: "loratadine and desethoxycarbonyl loratadine..." CLINICAL AND EXPERIMENTAL ALLERGY, vol. 27, no. 5, 1997, pages 559-567, XP000998792 page 564, column 1, line 1 -page 565, column 1, line 1	1-8

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims 1-8 relate to therapeutic applications which are actually not well defined. Use of the definitions "substantially returning work-related performance of a person suffering from an allergic and/or inflammatory condition of the skin or airway passages to the person's baseline work-related performance " in the present context is considered to lead to a lack of clarity within the meaning of Article 6 PCT.
The lack of clarity is such as to render a meaningful complete search not fully possible. Consequently, the search has been restricted to the the treatment of the diseases mentioned in claims 3 and 8.

Claims searched completely: none.
Claims searched incompletely: 1-8.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Interna[redacted] Application No
PCT/[redacted] 00/25609

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9848803 A	05-11-1998	AU 2407597 A	24-11-1998
		EP 0978281 A	09-02-2000
US 5900421 A	04-05-1999	AU 719907 B	18-05-2000
		AU 6434898 A	26-08-1998
		BR 9807673 A	15-02-2000
		CN 1246793 T	08-03-2000
		EP 1005345 A	07-06-2000
		NO 993847 A	27-09-1999
		WO 9834611 A	13-08-1998
		US 5962464 A	05-10-1999
		US 6054463 A	25-04-2000
WO 9834614 A	13-08-1998	AU 6271998 A	26-08-1998
		BR 9806157 A	09-01-2001
		CN 1246794 T	08-03-2000
		CZ 9901194 A	11-08-1999
		EP 0969836 A	12-01-2000
		HU 0001527 A	28-04-2001
		NO 992157 A	04-05-1999
		PL 334232 A	14-02-2000
		SK 47299 A	13-03-2000
		ZA 9800977 A	30-07-1998
US 4659716 A	21-04-1987	AT 61364 T	15-03-1991
		AU 638019 B	17-06-1993
		AU 5702690 A	04-10-1990
		AU 600665 B	23-08-1990
		AU 5737486 A	18-12-1986
		CA 1272480 A	07-08-1990
		CA 1307791 A	22-09-1992
		DE 3677842 D	11-04-1991
		DK 220986 A	14-11-1986
		EP 0208855 A	21-01-1987
		ES 554898 D	16-11-1987
		ES 8800679 A	01-02-1988
		FI 861987 A,B,	14-11-1986
		FI 87648 B	30-10-1992
		HK 75993 A	06-08-1993
		HU 41731 A,B	28-05-1987
		IE 59110 B	12-01-1994
		IL 78771 A	29-11-1990
		IL 91953 A	29-11-1990
		JP 2511412 B	26-06-1996
		JP 61289087 A	19-12-1986
		JP 2519880 B	31-07-1996
		JP 8059657 A	05-03-1996
		KR 9001853 B	24-03-1990
		PH 25101 A	19-02-1991
		PT 82570 A,B	01-06-1986
		SG 69193 G	06-08-1993
		AT 47140 T	15-10-1989
		AU 570306 B	10-03-1988
		AU 3993885 A	10-09-1985
		DE 3573600 D	16-11-1989
		DK 469485 A,B,	14-10-1985
		EP 0152897 A	28-08-1985
		FI 853675 A,B,	25-09-1985

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern[redacted] Application No
PCT/[redacted] 00/25609

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 4659716 A		HU 38332 A,B	28-05-1986
		JP 5072910 B	13-10-1993
		JP 61501205 T	19-06-1986
		LU 90738 A	09-05-2001
		WO 8503707 A	29-08-1985
WO 9806394 A	19-02-1998	AU 722040 B	20-07-2000
		AU 3973397 A	06-03-1998
		BR 9711149 A	17-08-1999
		CN 1233179 A	27-10-1999
		CZ 9900432 A	14-07-1999
		EP 0920315 A	09-06-1999
		HU 9904362 A	28-11-2000
		JP 2000505094 T	25-04-2000
		NO 990706 A	15-02-1999
		PL 331617 A	02-08-1999
		SK 20099 A	14-08-2000
		TR 9900326 T	21-05-1999
US 5595997 A	21-01-1997	AU 707541 B	15-07-1999
		AU 4512696 A	24-07-1996
		BR 9510129 A	30-12-1997
		CA 2208836 A	11-07-1996
		CN 1176598 A	18-03-1998
		CZ 9702026 A	18-03-1998
		DE 799037 T	05-10-2000
		EP 1078633 A	28-02-2001
		EP 0799037 A	08-10-1997
		ES 2144980 T	01-07-2000
		FI 972781 A	27-08-1997
		HU 77315 A	30-03-1998
		JP 10512240 T	24-11-1998
		NO 973023 A	19-08-1997
		SK 88897 A	04-02-1998
		WO 9620708 A	11-07-1996
		US 5731319 A	24-03-1998